

WHAT IS CLAIMED IS:

- 1 1. A miniature analytical device, comprising:
2 a body having a plurality of distinct reaction chambers disposed therein,
3 each of said reaction chambers being fluidly connected to at least one other of said
4 reaction chambers;
5 a sample inlet, fluidly connected to at least one of said plurality of reaction
6 chambers, for introducing a fluid sample into said device;
7 a fluid transport system for moving a fluid sample from at least a first
8 reaction chamber of said plurality of reaction chambers to at least a second reaction
9 chamber of said plurality of reaction chambers; and
10 a hybridization chamber for analyzing a component of said fluid sample,
11 said hybridization chamber being fluidly connected to at least one of said plurality of
12 reaction chambers and including a polymer array, said polymer array including a plurality
13 of different polymer sequences coupled to a surface of a single substrate, each of said
14 plurality of different polymer sequences being coupled to said surface in a different,
15 known location.
- 1 2. The device of claim 1, wherein each of said reaction chambers is
2 fluidly connected to at least one other of said reaction chambers by a fluid passage.
- 1 3. The device of claim 1, wherein each of said reaction chambers has
2 a cross sectional dimension of from about 0.5 to about 20 mm, and a depth dimension of
3 from about 0.5 to about 5 mm.
- 1 4. The device of claim 2, wherein said fluid passage has a cross-
2 sectional dimension of from about 20 m to about 1000 m, and a depth dimension of
3 from about 5 to 100 m.
- 1 5. The device of claim 1, wherein at least one of said reaction
2 chambers has a temperature controller disposed adjacent said reaction chamber, said
3 temperature controller including a heater for controlling a temperature of said reaction
4 chamber and a temperature sensor for monitoring a temperature of said reaction chamber.
- 1 6. The device of claim 1, wherein said body comprises at least three
2 distinct reaction chambers disposed therein.

1 7. The device of claim 1, wherein said body comprises at least four
2 reaction chambers disposed therein.

1 8. The device of claim 1, wherein said fluid transport system
2 comprises a micropump disposed in said body and fluidly connected to at least one of
3 said plurality of reaction chambers.

1 9. The device of claim 8, wherein said micropump is disposed within
2 a central pumping chamber in said body, said central pumping chamber being fluidly
3 connected to each of said plurality of reaction chambers by one of a plurality of fluid
4 passages, each of said plurality of fluid passages including a valve disposed across said
5 fluid passage, whereby said fluid passages may be selectively opened and closed to
6 direct a fluid sample from a first of said plurality of reaction chambers through said
7 central pumping chamber and into a second of said plurality of reaction chambers.

1 10. The device of claim 1, wherein said plurality of distinct reaction
2 chambers are fluidly connected in a series.

1 11. The device of claim 1, wherein said polymer array comprises at
2 least 100 different polymer sequences coupled to said surface of said single substrate,
3 each of said plurality of different polymer sequences being coupled to said surface in a
4 different, known location.

1 12. The device of claim 1, wherein said polymer array comprises at
2 least 1000 different polymer sequences coupled to said surface of said single substrate,
3 each of said plurality of different polymer sequences being coupled to said surface in a
4 different, known location.

1 13. The device of claim 1, wherein said polymer array comprises at
2 least 10,000 different polymer sequences coupled to said surface of said single substrate,
3 each of said plurality of different polymer sequences being coupled to said surface in a
4 different, known location.

1 14. The device of claim 1, wherein said plurality of different polymer
2 sequences are a plurality of different nucleic acid sequences.

1 15. The device of claim 1, wherein at least one of said plurality of
2 reaction chambers comprises a nucleic acid fragmentation system, for fragmenting a
3 nucleic acid in a fluid sample.

1 16. The device of claim 15, wherein said fragmentation system
2 comprises:

3 a series of microstructures fabricated on a first surface of said reaction
4 chamber; and

5 a piezoelectric element attached to an external surface of said body
6 adjacent said first surface of said reaction chamber.

1 17. The device of claim 15, wherein said fragmentation system
2 comprises at least one channel through which said fluid sample is pumped, said channel
3 having a submicron cross-sectional dimension for generating a high-shear rate.

1 18. A miniature analytical device, comprising:

2 a body having a plurality of distinct reaction chambers disposed therein,
3 each of said reaction chambers being fluidly connected to at least one other of said
4 reaction chambers;

5 a sample inlet, fluidly connected to at least one of said plurality of reaction
6 chambers, for introducing a fluid sample into said device;

7 a fluid transport system for moving a fluid sample from at least a first
8 reaction chamber of said plurality of reaction chambers to at least a second reaction
9 chamber of said plurality of reaction chambers; and

10 a microcapillary channel for analyzing a component of said fluid sample,
11 said microcapillary channel being fluidly connected to at least one of said plurality of
12 reaction chambers and including at least first and second electrodes at opposite ends of
13 said microcapillary channel for applying a voltage across said microcapillary channel.

1 19. The miniature device of claim 18, wherein each of said reaction
2 chambers has a cross sectional dimension of from about 0.5 to about 20 mm, and a depth
3 dimension of from about 0.05 to about 5 mm.

1 20. The device of claim 18, wherein at least one of said reaction
2 chambers has a temperature controller disposed adjacent said reaction chamber, said

3 temperature controller including a heater for controlling a temperature of said reaction
4 chamber and a temperature sensor for monitoring a temperature of said reaction chamber.

1 21. The device of claim 18, wherein at least one of said plurality of
2 distinct reaction chambers comprises an extension reaction chamber fluidly connected to
3 said microcapillary channel, said extension reaction chamber having disposed therein, one
4 or more reagents selected from the group consisting of a DNA polymerase,
5 deoxynucleoside triphosphates and dideoxynucleoside triphosphates.

1 22. The device of claim 21, further comprising four microcapillary
2 channels and four extension reaction chambers, each of said microcapillary channels
3 being fluidly connected to a separate one of said four extension reaction chambers, each
4 of said separate extension reaction chambers having disposed therein a different
5 dideoxynucleoside triphosphate.

1 23. A miniature analytical device, comprising:

2 a body having a plurality of distinct reaction chambers disposed therein, at
3 least one of said reaction chambers being an in vitro transcription reaction chamber, said
4 in vitro transcription reaction chamber having an effective amount of an RNA polymerase
5 and four different nucleoside triphosphates, disposed therein;

6 a sample inlet, fluidly connected to at least one of said plurality of reaction
7 chambers, for introducing a fluid sample into said device; and

8 a fluid transport system for moving a fluid sample from at least a first
9 reaction chamber of said plurality of reaction chambers to at least a second reaction
10 chamber of said plurality of reaction chambers.

1 24. The device of claim 22, wherein said in vitro transcription reaction
2 chamber has a temperature controller disposed adjacent said transcription reaction
3 chamber, said temperature controller including a heater for controlling a temperature of
4 said reaction chamber and a temperature sensor for monitoring a temperature of said
5 reaction chamber.

1 25. The device of claim 23, wherein at least one of said reaction
2 chambers has a polymer array disposed therein, said polymer array including a plurality
3 of different polymer sequences coupled to a surface of a single substrate, each of said

4 plurality of different polymer sequences being coupled to said surface in a different,
5 known location.

1 26. A miniature analytical device, comprising:
2 a body having at least first, second and third reaction chambers disposed
3 within said body;

4 said first reaction chamber having an opening disposed through said body
5 for introducing a fluid sample into said first reaction chamber, said second reaction
6 chamber having disposed therein at least one reagent for amplifying a nucleic acid
7 segment within a sample, and said third reaction chamber having an array of
8 oligonucleotides disposed therein, said array including a plurality of different nucleic acid
9 sequences coupled to a surface of a single substrate, each of said plurality of different
10 nucleic acid sequences being coupled to said surface in a different, known location, and
11 disposed within said third chamber for hybridizing with at least a portion of a nucleic acid
12 segment amplified in said second reaction chamber; and

13 a fluid transport system for transporting a fluid sample from said first
14 reaction chamber to said second reaction chamber and from said second reaction chamber
15 to said third reaction chamber.

1 27. The miniature device of claim 26, wherein each of said reaction
2 chambers is fluidly connected to at least one other of said reaction chambers by a fluid
3 passage.

1 28. The miniature device of claim 26, wherein each of said reaction
2 chambers has a cross sectional dimension of from about 0.5 to about 20 mm, and a depth
3 dimension of from about 0.05 to about 5 mm.

1 29. The miniature device of claim 27, wherein said fluid passage has a
2 cross-sectional dimension of from about 20 m to about 1000 m, and a depth dimension
3 of from about 5 to 100 m.

1 30. The device of claim 26, wherein said second reaction chamber
2 comprises a temperature controller adjacent said second reaction chamber for controlling
3 a temperature within said second reaction chamber.

1 31. The device of claim 26, wherein said temperature controller
2 comprises a heating element disposed within said second reaction chamber for controlling

3 said temperature of said second reaction chamber and a temperature sensor for monitoring
4 said temperature of said second reaction chamber.

1 32. The device of claim 26, wherein said fluid transport system
2 comprises a micropump disposed in said body and fluidly connected to at least one of
3 said plurality of reaction chambers.

1 33. The device of claim 26, wherein said array of oligonucleotides
2 comprises at least 100 different nucleic acid sequences coupled to said surface of said
3 single substrate, each of said plurality of different nucleic acid sequences being coupled
4 to said surface in a different, known location.

1 34. The device of claim 26, wherein said array of oligonucleotides
2 comprises at least 1000 different nucleic acid sequences coupled to said surface of said
3 single substrate, each of said plurality of different nucleic acid sequences being coupled
4 to said surface in a different, known location.

1 35. The device of claim 26, wherein said array of oligonucleotides
2 comprises at least 10,000 different nucleic acid sequences coupled to said surface of said
3 single substrate, each of said plurality of different nucleic acid sequences being coupled
4 to said surface in a different, known location.

1 36. The device of claim 26, wherein said body further comprises a
2 transparent region disposed over said third reaction chamber for determining
3 hybridization of said nucleic acid in said sample to said oligonucleotide array.

1 37. A miniature analytical device, comprising:

2 a body having at least three distinct reaction chambers disposed therein,
3 wherein each of said reaction chambers is fluidly connected to at least one other of said
4 reaction chambers;

5 a first of said reaction chambers including a cell lysis system disposed
6 therein, for lysing cells in a fluid sample;

7 a second of said reaction chambers having amplification reagents disposed
8 therein, for amplifying a nucleic acid derived from said cells lysed in said first reaction
9 chamber;

10 a third reaction chamber having an oligonucleotide array disposed therein,
11 said oligonucleotide array including a plurality of different nucleic acid sequences

12 coupled to a surface of a single substrate, each of said plurality of different nucleic acid
13 sequences being coupled to said surface in a different, known location;
14 a sample inlet, fluidly connected to at least one of said plurality of reaction
15 chambers, for introducing a fluid sample into said device; and
16 a fluid transport system for moving a fluid sample from said at least first
17 reaction chamber to said at least second reaction chamber, and from said at least second
18 reaction chamber to said at least third reaction chamber.

1 38. The miniature device of claim 37, wherein each of said reaction
2 chambers is fluidly connected to at least one other of said reaction chambers by a fluid
3 passage.

1 39. The miniature device of claim 37, wherein each of said at least
2 first, second and third reaction chambers has a cross sectional dimension of from about
3 0.5 to about 20 mm, and a depth dimension of from about 0.05 to about 5 mm.

1 40. The miniature device of claim 38, wherein said fluid passage has a
2 cross-sectional dimension of from about 20 m to about 1000 m, and a depth dimension
3 of from about 5 to 100 m.

1 41. The device of claim 37, wherein at least one of said reaction
2 chambers has a temperature controller disposed adjacent said reaction chamber, said
3 temperature controller including a heater for controlling a temperature of said reaction
4 chamber and a temperature sensor for monitoring a temperature of said reaction chamber.

1 42. The device of claim 37, wherein said fluid transport system
2 comprises a micropump disposed in said body and fluidly connected to at least one of
3 said plurality of reaction chambers.

1 43. The device of claim 37, wherein said cell lysis system comprises a
2 series of pointed microstructures on a surface of said at least first reaction chamber, for
3 piercing cells in said fluid sample.

1 44. The device of claim 37, wherein said cell lysis system comprises an
2 ultrasonic generator adjacent said at least first reaction chamber, for disrupting cells in
3 said fluid sample.

1 45. A miniature analytical device, comprising:
2 a body having a plurality of distinct reaction chambers disposed therein,
3 each of said reaction chambers being fluidly connected to at least one other of said
4 reaction chambers, at least one of said reaction chambers being a temperature controlled
5 reaction chamber having a controllable heating element disposed therein;
6 a sample inlet, fluidly connected to at least one of said plurality of reaction
7 chambers, for introducing a fluid sample into said device; and
8 a fluid transport system for moving a fluid sample from at least a first
9 reaction chamber of said plurality of reaction chambers to at least a second reaction
10 chamber of said plurality of reaction chambers.

1 46. The miniature device of claim 45, wherein each of said reaction
2 chambers is fluidly connected to at least one other of said reaction chambers by a fluid
3 passage.

1 47. The miniature device of claim 45, wherein each of said at least
2 first, second and third reaction chambers has a cross sectional dimension of from about
3 0.5 to about 20 mm, and a depth dimension of from about 0.05 to about 5 mm.

1 48. The miniature device of claim 46, wherein said fluid passage has a
2 cross-sectional dimension of from about 20 m to about 1000 m, and a depth dimension
3 of from about 5 to 100 m.

1 49. The device of claim 45, wherein said heating element is a resistive
2 heating element.

1 50. The device of claim 49, wherein said resistive heating element is a
2 NiCr/polyimide/copper laminate heating element.

1 51. The device of claim 45, further comprising a temperature sensor
2 disposed within said temperature controlled reaction chamber.

1 52. The device of claim 51, wherein said temperature sensor is a
2 thermocouple.

1 53. The device of claim 45, wherein at least one of said at least first
2 and second reaction chambers has a polymer array disposed therein, said polymer array

3 including a plurality of different polymer sequences coupled to a surface of a single
4 substrate, each of said plurality of different polymer sequences being coupled to said
5 surface in a different, known location.

1 54. The device of claim 53, wherein said plurality of different polymer
2 sequences are a plurality of different nucleic acid sequences.

1 55. A miniature analytical device, comprising:
2 a body having a plurality of distinct reaction chambers disposed therein,
3 each of said reaction chambers being fluidly connected to at least one other of said
4 reaction chambers;

5 a fluid mixing system for generating convection within at least one of said
6 reaction chambers;

7 a sample inlet, fluidly connected to at least one of said plurality of reaction
8 chambers, for introducing a fluid sample into said device; and

9 a fluid transport system for moving a fluid sample from at least a first
10 reaction chamber of said plurality of reaction chambers to at least a second reaction
11 chamber of said plurality of reaction chambers.

1 56. The miniature device of claim 55, wherein each of said at least
2 first, second and third reaction chambers is fluidly connected to at least one other of said
3 reaction chambers by a fluid passage.

1 57. The miniature device of claim 55, wherein each of said at least
2 first, second and third reaction chambers has a cross sectional dimension of from about
3 0.5 to about 20 mm, and a depth dimension of from about 0.05 to about 5 mm.

1 58. The miniature device of claim 56, wherein said fluid passage has a
2 cross-sectional dimension of from about 20 m to about 1000 m, and a depth dimension
3 of from about 5 to 100 m.

1 59. The device of claim 55, wherein said mixing system comprises a
2 piezoelectric element attached to an external surface of said body adjacent said at least
3 one reaction chamber, whereby activation of said piezoelectric element creates a
4 convective effect within said reaction chamber.

1 60. The device of claim 55, wherein said mixing system comprises:
2 a plurality of metallic particles disposed within said at least one reaction
3 chamber;

4 an electromagnetic field generator adjacent said at least one reaction
5 chamber, whereby when said electromagnetic field generator is activated, said metallic
6 particles are vibrated within said at least one reaction chamber mixing contents of said
7 reaction chamber.

1 61. The device of claim 55, wherein said mixing system comprises a
2 micropump disposed within a pumping chamber in said body, said pumping chamber
3 being fluidly connected to said at least one of said reaction chamber, an operation of said
4 micropump creating convection in said at least one of said reaction chambers.

1 62. The device of claim 55, wherein at least one of said reaction
2 chambers has a polymer array disposed therein, said polymer array including a plurality
3 of different polymer sequences coupled to a surface of a single substrate, each of said
4 plurality of different polymer sequences being coupled to said surface in a different,
5 known location.

1 63. The device of claim 62, wherein said plurality of different polymer
2 sequences are a plurality of different nucleic acid sequences.

1 64. A miniature analytical device, comprising:
2 a body having a plurality of distinct reaction chambers disposed therein;
3 a sample inlet, fluidly connected to at least one of said plurality of distinct
4 reaction chambers, for introducing a fluid sample into said device;
5 a central pumping chamber disposed within said body, said central
6 pumping chamber being fluidly connected to each of said plurality of reaction chambers
7 by one of a plurality of fluid passages, each of said plurality of fluid passages including a
8 valve disposed across said fluid passage, whereby said fluid passages may be selectively
9 opened and closed to direct a fluid sample from a first of said plurality of reaction
10 chambers through said central pumping chamber and into a second of said plurality of
11 reaction chambers.

1 65. The miniature device of claim 64, wherein each of said reaction
2 chambers has a cross sectional dimension of from about 0.5 to about 20 mm, and a depth
3 dimension of from about 0.05 to about 5 mm.

1 66. The miniature device of claim 64, wherein said fluid passage has a
2 cross-sectional dimension of from about 20 m to about 1000 m, and a depth dimension
3 of from about 5 to 100 m.

1 67. The device of claim 64, wherein at least one of said reaction
2 chambers includes amplification reagents disposed therein, for amplifying a nucleic acid
3 in said fluid sample.

1 68. The device of claim 64, wherein at least one of said at least first
2 and second reaction chambers includes an oligonucleotide array disposed therein, said
3 oligonucleotide array including a plurality of different nucleic acid sequences coupled to
4 a surface of a single substrate, each of said plurality of different nucleic acid sequences
5 being coupled to said surface in a different, known location.

1 69. A miniature analytical device, comprising:

2 a body having at least a first reaction chamber fluidly connected to a
3 second reaction chamber by a fluid passage;

4 a sample inlet, fluidly connected to said first reaction chamber, for
5 introducing a fluid sample into said device;

6 a differential pressure delivery system for maintaining said first reaction
7 chamber at a first pressure and said second reaction chamber at a second pressure, said
8 first pressure being greater than ambient pressure and said second pressure being greater
9 than said first pressure, whereby when said second reaction chamber is brought to
10 ambient pressure, said first pressure forces a liquid sample in said first reaction chamber
11 into said second reaction chamber.

1 70. The miniature device of claim 66, wherein each of said at least first
2 and second reaction chambers has a cross sectional dimension of from about 0.5 to about
3 20 mm, and a depth dimension of from about 0.05 to about 5 mm.

1 71. The miniature device of claim 69, wherein said fluid passage has a
2 cross-sectional dimension of from about 20 m to about 1000 m, and a depth dimension
3 of from about 5 to 100 m.

1 72. The device of claim 69, wherein said differential pressure delivery
2 system comprises:

3 a pressure source;

4 at least first and second passages fluidly connecting said pressure source to
5 said at least first and second reaction chambers, respectively;

6 a first fluidic resistance disposed in said first passage between said
7 pressure source and said first reaction chamber, said first fluidic resistance transforming a
8 pressure from said pressure source to said first pressure;

9 a second fluidic resistance disposed in said second passage between said
10 pressure source and said second reaction chamber, said second fluidic resistance
11 transforming said pressure from said pressure source to said second pressure; and

12 first and second openable closures in said first and second reaction
13 chambers, respectively, whereby opening of said first or second closures allows said first
14 or second reaction chambers to achieve ambient pressure.

1 73. The miniature device of claim 72, wherein said first and second
2 fluidic resistances independently comprise one or more fluid passages connecting said
3 first and second passages to said first and second reaction chambers, said first fluidic
4 resistance having a smaller cross-sectional area than said second fluidic resistance.

1 74. A miniature analytical device, comprising:

2 a body having at least a first reaction chamber fluidly connected to a
3 second reaction chamber;

4 a sample inlet, fluidly connected to said first reaction chamber, for
5 introducing a fluid sample into said device;

6 a differential pressure delivery source for maintaining said first reaction
7 chamber at a first pressure and said second reaction chamber at a second pressure, said
8 second pressure being less than ambient pressure and said first pressure being less than
9 said second pressure, whereby when said first reaction chamber is brought to ambient
10 pressure, said second pressure draws a liquid sample in said first reaction chamber into
11 said second reaction chamber.

1 75. The device of claim 74, wherein said at least a first reaction
2 chamber is fluidly connected to said second reaction chamber by a fluid passage.

1 76. The miniature device of claim 74, wherein each of said reaction
2 chambers has a cross sectional dimension of from about 0.5 to about 20 mm, and a depth
3 dimension of from about 0.05 to about 5 mm.

1 77. The miniature device of claim 75, wherein said fluid passage has a
2 cross-sectional dimension of from about 20 m to about 1000 m, and a depth dimension
3 of from about 5 to 100 m.

1 78. The device of claim 75, wherein said differential pressure delivery
2 system comprises:

3 a pressure source;

4 at least first and second passages fluidly connecting said pressure source to
5 said at least first and second reaction chambers, respectively;

6 a first fluidic resistance disposed in said first passage between said
7 pressure source and said first reaction chamber, said first fluidic resistance transforming a
8 pressure from said pressure source to said first pressure;

9 a second fluidic resistance disposed in said second passage between said
10 pressure source and said second reaction chamber, said second fluidic resistance
11 transforming said pressure from said pressure source to said second pressure; and

12 first and second openable closures in said first and second reaction
13 chambers, respectively, whereby opening of said first or second closures allows said first
14 or second reaction chambers to achieve ambient pressure.

1 79. The miniature device of claim 78, wherein said first and second
2 fluidic resistances independently comprise one or more fluid passages connecting said
3 first and second passages to said first and second reaction chambers, said first fluidic
4 resistance having a larger cross-sectional area than said second fluidic resistance.

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